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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,416	11/28/2000	Hong Jin	7682-052-999	7604

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EXAMINER
BRUMBACK, BRENDA G

ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 06/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/724,416	Applicant(s) JIN ET AL.	
	Examiner Brenda G. Brumback	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cov r sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-16,19-21,33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-18, 22-32, and 35-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2 and 9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group VI, claims 17, 18, 22-32, and 35, in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the search for the vaccines is cumulative in scope with a search for the respective RSV's and that Groups V and VI have the same classification. This is not found persuasive because in contrast to applicant's assertion, the required searches for the vaccine compositions and for the RSV's are not the same search, as is evidenced by their separate classifications. The RSV's of Groups V and VI have different and distinct structures and for this reason, each of these groups requires a different search strategy. Rejoinder of the groups would thus constitute a serious burden upon the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The Information Disclosure Statements filed 03/02/2001 and 03/22/2001 are acknowledged. Signed copies of the PTO-1449 forms are attached hereto.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, Provisional Application number 60/060,153, upon which priority is claimed, fails to provide adequate support under 35 U.S.C. 112 for claims 17-18, 22-32, and 35 of this application. For purposes of examination, priority has been established as 05/04/1998, as claims 17-18, 22-32, and 35 appear to be supported by Provisional Application Number 60/084,133, filed 05/04/98.

Claim Rejections - 35 USC § 112

Claims 17-18, 22-32, and 35-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vaccine compositions for inducing protective immunity in mammals other than humans, does not reasonably provide enablement for vaccine compositions which induce protective immunity in humans. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to vaccine compositions comprising an attenuated respiratory syncytial virus (RSV) with one or more gene deletions. The claims thus encompass conferring a protective immune response in humans against RSV disease.

The state of the prior art and the predictability or lack thereof in the art: While the art teaches that RSV vaccine compositions comprising attenuated RSV with one or more gene deletions may replicate *in vivo* and elicit antibody production in the host (see Bukreyev et al., Journal of Virology 71/12:8973-8982, December 1997, especially the abstract), the art teaches that to date RSV vaccines have been ineffective for eliciting a protective immune response against disease in humans (see Murphy et al., Virus Research 32:13-36, 1994, especially pages 14-15 and 22-26)

The amount of direction or guidance present and the presence or absence of working examples: Given the teachings of unpredictability found in the art regarding the protective efficacy of RSV vaccines in humans, detailed teachings are required to be present in the specification in order to enable one of skill in the art to be able to use the claimed vaccines to confer protection against RSV disease in a human subject. Such teachings are absent. The specification discloses and provides working examples describing inoculation of the RSV components of the claimed composition into cotton rats and African green monkeys in order to elicit antibody production (see pages 111-113). The art teaches, however, that protective immunity in rodents and African green monkeys is not predictive of RSV vaccine efficacy in humans. See for example, Murphy et al., the sentence bridging pages 23-24, wherein Murphy et al. state " ... that it is relatively easy to protect rodents and monkeys which are only semi-permissive for RSV infection, but it is more difficult to protect ... a fully permissive host".

The breadth of the claims and the quantity of experimentation needed: Because the claims are drawn to vaccine compositions which have been interpreted as encompassing elicitation of a protective immune response against RSV disease in humans, because the art teaches that RSV vaccines are ineffective for conferring such a protective immune response in humans, and because the specification

fails to contain sufficient disclosure to overcome the teachings of unpredictability found in the art, it would require undue experimentation by one of skill in the art to be able to use the claimed composition for eliciting protective immunity in a human host commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 17-18, 22-32, and 35-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins (WO 97/ 12032, of record as an IDS reference).

The claimed invention is drawn to a vaccine composition comprising a respiratory syncytial virus (RSV) the genome of which contains the reverse complement of an mRNA coding sequence operatively linked to a polymerase binding site of a RSV comprising either a deletion of one or more genes selected from M2-2, SH, NS1, and NS2 or an mRNA coding sequence encoding G and F genes of both RSV subgroups A and B, and a pharmaceutically acceptable carrier.

Collins teaches vaccine compositions comprising RSV genomes and anti-genomes having functional deletion (ablation) of the NS1, NS2, SH, and/or M2(ORF2) genes and a pharmaceutical carrier (see the abstract and page 20, lines 6-25). Collins teaches that the RSV genomes and anti-genome can be modified to include nucleotide sequences encoding F and G proteins of different RSV subgroups (see page 5, lines 16-20, and page 21, lines 19-32). Collins teaches that the RSV subgroups are designated as A and B (see page 6, line 34, through page 7, line 7). Collins teaches that inclusion of the G protein gene of RSV subgroup B broadens the response to vaccines comprising the chimeric virus particles to cover a wider spectrum of the relatively diverse subgroup A and B strains present in the human population (see page 19, lines 1-15).

Claims 17-18, 22-32, and 35-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Murphy et al. (U.S. Patent 5,993,824).

The claimed invention is as described *supra*.

Murphy et al. teach attenuated vaccine compositions comprising RSV particles with specific mutations or deletions in any of the M2 ORF2, SH, NS1 or NS2 viral accessory genes or any combination of the M2 ORF2, SH, NS1 and NS2 genes. Murphy et al. teach that mutations in or deletions of one or more of the genes results in enhanced growth in tissue culture (the SH gene deletion), enhanced attenuation, and/or enhanced genetic resistance to reversion from an attenuated phenotype (see the abstract; column 5, lines 18-25 and 54-57; column 6, lines 1-43; column 17, lines 33-36; column 18, lines 9-16 and 26-28). Murphy et al. also teach incorporation of the F and G protective antigens from one RSV strain or subgroup into an RSV clone of the heterologous subgroup or strain of RSV so as to stimulate a cross-protective immune response against both strains or subgroups (see column 6, lines 36-61).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-18, 22-32, and 35-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al. (Proc. Natl. Acad. Sci. 92:11563-11567, December 1995, of record as IDS reference) in view of Olmsted et al. (Proc. Natl. Acad. Sci. 83:7462-7466, October 1986).

The claimed invention is as described *supra*.

Collins et al. teach an isolated infectious RSV particle comprising cDNA encoding a complete positive-sense anti-genome operatively linked to the promoter for T7 RNA polymerase, a hammerhead ribozyme, and tandem terminators of T7 transcription (see the abstract and page 11564, second full paragraph bridging columns 1 and 2). Collins et al. teach that one or more of the M2-2, SH, NS1 and NS2 genes can be deleted or ablated for development of vaccines with modified growth in tissue culture and/or for attenuation (see page 11566, the paragraph bridging columns 1 and 2). Finally, Collins et al. teach a chimeric virus incorporating genes of RSV subgroup B into subgroup A particles, in order to broaden the vaccine response to cover a wider spectrum of the relatively diverse subgroup A and B strains present in the human population (see page 11567, last paragraph). Collins 1995 does not specifically teach the infectious particles as comprising coding sequences for the F and G genes from both subgroups A and B.

Olmsted et al. teach that the major viral antigens responsible for inducing protective antibodies against RSV are the F and G glycoproteins (see page 7462, the abstract and the paragraph bridging columns 1 and 2).

One of ordinary skill in the art at the time the invention was made would have found it *prima facie* obvious to have incorporated both the F and G genes from both RSV A and RSV B into a single recombinant virus in order to broaden the vaccine response to cover both strains.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner cannot be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Official FAX telephone number is (703) 872-9306 and the After Final FAX telephone number is (703) 872-9307. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Brenda Brumback
Patent Examiner